With respect to the restriction requirement, Applicants greatly appreciate the Examiner's modification to permit examination of Group VII with the elected Group I and her confirmation that the right of rejoinder would be applicable to this case.

To advance prosecution towards an early allowance in view of the restriction being made final and the possibility of rejoinder of the process claims, the current amendment cancels nonelected Claims 11-14, 17, 29 and 30 without prejudice to filing a divisional application drawn to the subject matter of these claims, and keeps withdrawn process Claims 23-38 in the application. Nonelected Claim 31 has also been retained in this case to give the Examiner the opportunity to reconsider its relationship with the subject matter of Claims 5 and 16 relevant to the new mutation of the present invention and, thus, for further consideration on the merits.

The Examiner applied a provisional double patenting rejection of Claims 1-4, 6-10, 15(a-c), 18-22 and 32 under 35 U.S.C. § 101 as claiming the same invention as that of Claims 1-9, 13 (a-c), 14-18 and 25 of co-pending Application No. 10/314,512. Applicants are promptly amending the conflicting claims in both cases so the claims are no longer coextensive in scope. The amendments will obviate the provisional double patenting rejection.

The Examiner has rejected Claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement for reasons given on pages 6 and 7 of the Office action. Applicants respectfully traverse the rejection.

The written description of the mutations in no uncertain terms makes it perfectly clear that the subject matter recited in Claim 5 was adequately described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner's attention is respectfully drawn to the specification from page 19, line 21 to page 20, line 2 which states:

> Two novel amino acid mutations are identified in the capsid gene after 120 passages, and it is shown that these two mutations are responsible for the increased growth rate *in vitro* and the attenuation of virulence *in vivo*. There are only two nucleotide differences as well, cytosine to guanine (C to G) and adenine to cytosine (A to C), both of which are non-silent mutations that result in the two amino acid changes. The first mutation occurs at passage 30, in which a proline at position 110 of the capsid protein is substituted for an alanine (P110A), and this mutation remains in the subsequent passages. In position 328 of the

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nucleotide sequence, cytosine changes to guanine (C to G) leading to this amino acid change of P110A. The second mutation, a substitution of an arginine for a serine at position 191 of the capsid protein (R191S), appears at passage 120 but not in earlier passages. In nucleotide position 573, adenine changes to cytosine (A to C) leading to this second amino acid change of R191S.

Figure 10 representing the 702 bp (699 bp sequence plus the 3 nucleotide stop codon) DNA sequence of the original immunogenic ORF2 capsid gene of the cloned chimeric PCV1-2 DNA (which corresponds to SEQ ID NO:3) shows cytosine in position 328 of the nucleotide sequence of the ORF2 and adenine in position 573 before mutation from C to G and A to C, respectively. (Instead of Figure 10, the Examiner may find that looking at SEQ ID NO:3 in the Sequence Listing is easier to see the exact nucleotide positions 328 and 573 in the capsid gene used in the illustration of the present method.)

In sum, Applicants fully describe the sequence changes in the original ORF2 gene from C to G in nucleotide position 328 and from A to C in nucleotide position 573. These mutations are even exemplified by actual working examples in Examples 21-24 on pages 72-85 of the specification. One of ordinary skill in the art would not question the assertions or results. It is certain that the ordinary practitioner would conclude that there is adequate disclosure of the mutations claimed.

In view of the foregoing remarks, Applicants respectfully ask that the rejection of Claim 5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Examiner has rejected Claims 7 and 10 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement for reasons given on pages 7 and 8 of the Office action.

To fulfill the statutory obligation, it is hereby averred that the deposit of the plasmid containing the chimeric PCV1-2 DNA clone, assigned ATCC Patent Deposit Designation PTA-3912, has been deposited in the ATCC on December 7, 2001 under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. A true copy of the deposit receipt further evidencing that the deposit was made pursuant to the Budapest Treaty is attached hereto.

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Since the deposit conditions satisfy the statutory requirements, Applicants respectfully ask that the Examiner withdraw the rejection of Claims 7 and 10 under 35 U.S.C. § 112, first paragraph.

The Examiner has rejected Claims 15(a-c), 16 and 18-22 under 35 U.S.C. § 112, first paragraph, because, in the Examiner's opinion, the specification is enabling only for protecting a pig against PMWS with a chimeric PCV1-2 but does not reasonably provide enablement for treating PCV2 associated disease with PCV1-2 or preventing or treating PCV2 infection with a PCV2-1 chimera or any chimeric circovirus for reasons given on pages 8 and 9 of the Office action. Applicants respectfully traverse the rejection in part but note that the present amendment will obviate most of the rejection.

In particular, the claims have been amended for the better readability thereof, to make clear that the present invention includes the live chimeric viruses derived from the chimeric PCV1-2 DNA clones described herein that are useful as vaccines (see the specification on page 24, lines 14-28). The amendment to Claim 15 (c) is found in the specification on page 12, lines 2-6, and page 18, lines 13-18.

Insofar as the traversal is concerned, it is submitted that Applicants are not claiming a method of treating PCV2 associated disease or infection with any of their new constructs, PCV1-2, PCV2-1 or chimeric circoviruses. Rather, the invention described in the application is drawn to a vaccine for providing protection to a pig against infection or PMWS disease caused by PCV2 (see the specification on page 15, lines 24-27). Vaccination is a preventative measure to prevent the infection or disease from taking hold or occurring in the first place; Applicants do not teach or imply that the vaccine is to be directly used as a treatment once the pig has already developed the PCV2 infection or disease. Therefore, the Examiner's concerns are not justified by the circumstances of this case.

In view of the foregoing comments and the amendment, Applicants respectfully request that the rejection of Claims 15(a-c), 16 and 18-22 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Examiner has rejected Claims 1-3 and 32 under 35 U.S.C. § 103 as allegedly being unpatentable over Allan *et al.* (U.S. Patent No. 6,217,883 B1) in view of Caggana *et al.* (Journal of Virology, 1993), Lustig *et al.* (Journal of Virology, 1988) and Mahé *et al.* (Journal of General

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Virology, 2000) for reasons given on pages 10 and 11 of the Office action. Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, the guidelines of M.P.E.P. § 706.02(j) and case law provide three basic criteria: (1) There must be some suggestion or motivation to modify the reference or to combine the reference teachings; (2) there must be a reasonable expectation of success; and (3) the combined references must teach or suggest all claim limitations. In the case at hand, the *prima facie* case of obviousness is not established because the combined art fails to meet all three factors.

Allan *et al.* disclose a combination vaccine against PMWS comprising at least one PCV2 antigen and one porcine parvovirus antigen in which the PCV2 antigen may comprise a vector expressing an antigen encoded by any one of ORF1-13. As the Examiner understands, Allan *et al.* do not teach how to generate a chimeric nucleic acid molecule of PCV1-2 that uses an ORF gene of the pathogenic PCV2 within the backbone structure of the PCV1 nucleic acid molecule as recited in Claims 1-3, or the reciprocal chimeric nucleic acid molecule of PCV2-1 as recited in Claim 32. To arrive at the present invention, there must be some suggestion or motivation to modify Allan *et al.* or combine the teachings of Allan *et al.* with the secondary references. It is clear that the suggestion or motivation to make any sort of chimeric PCV2, let alone Applicants' chimeric PCV1-2, is totally lacking in Allan *et al.* and, thus, the rest of the cited art must be examined for what they teach the ordinary practitioner.

Caggana *et al.* concern the study of the genetic basis of the virulence of the picornaviruses, which comprise single-stranded RNA viruses, using recombinant, chimeric viruses. Lustig *et al.* relate to the study of the differences in neurovirulence of the Sindbis virus, a member of the family *Togaviridae*, which is also an RNA virus. In sharp contrast, the porcine circoviruses are DNA viruses. The chimeric constructs of the RNA viruses taught by Caggana *et al.* and Lustig *et al.*, therefore, are not analogous to the chimeric DNA virus of the present invention. Because a chimeric virus from the *Picornaviridae* or *Togaviridae* families with an RNA genome can be made and attenuated, one of ordinary skill in the art could not predict or deduce from Caggana *et al.* or Lustig *et al.* that the chimeric construct and attenuation property would also be true in the *Circoviridae* family, a DNA virus family. The ordinary practitioner would not have a reasonable expectation of success based on the meaningless teachings of Caggana *et al.* and Lustig *et al.*

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With respect to Mahé *et al.*, the article reports on the identification of immunorelevant epitopes of PCV1 and PCV2, and their findings that the ORF1 proteins were antigenically related in the two PCV types. In the second column of page 1822, the authors further indicate their results of investigating immunoreactivity against the putative capsid protein encoded by the major ORF2. They state that a hyperimmune serum generated against ORF2 from PCV2 did not allow the detection of viral protein in PCV1-transfected cells. They were able to identify antigenic domains in the ORF2-PCV2 proteins along with a few reactive proteins common to ORF2 from PCV1 and PCV2. However, the authors were only concerned with the potential use of ORF2-derived antigens as diagnostic tools or reagents in the development of an immunoassay such as ELISA for the detection of PCV2 infection in herds.

While the results of Mahé *et al.* indicate cross-reactivity of PCV1 and PCV2 ORF2 protein, it is also interesting to note that PCV1 is not pathogenic while PCV2 is pathogenic and causes PMWS in pigs. Most importantly, prior mild PCV1 infection does not protect against the more serious PCV2 infection. The ordinary practitioner, as a consequence, would not be motivated to use nonpathogenic PCV1 as an antigen in a vaccine against PMWS because it is not likely to be effective in eliciting an immune reaction to PCV2 or infections caused by PCV2.

It is clear that there is absolutely no suggestion or teaching by Allan *et al.* in view of Mahé *et al.* to combine parts of the molecular structures of PCV1 and PCV2 into a practical chimeric vaccine comprising the chimeric PCV1-2 or to prepare the reciprocal PCV2-1 constructs. All claim limitations are neither suggested nor taught by the combined references. Indeed, Applicants believe that they are the first to design a chimeric virus construct in the *Circoviridae* family, DNA viruses unlike the chimeric RNA viruses previously published. Without any doubt, the unique chimeric porcine circoviruses of the present invention are not obvious from the cited art.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-3 and 32 under 35 U.S.C. § 103, and allow the application to issue as a patent.

If any outstanding issue remains in this case, the Examiner is invited to contact the undersigned attorney by phone or e-mail to discuss mutually agreeable solutions.

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Accordingly, it is believed that this application is now in condition for an allowance. Favorable treatment is respectfully urged.

Respectfully submitted,

VIRGINIA TECH INTELLECTUAL PROPERTIES, INC. and IOWA STATE UNIVERSITY RESEARCH FOUNDATION, INC.

Date: December 7, 2005 By: Anne M Rosenblum

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AMENDED

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Virginia Polytechnic Institute and State University
Attn: Xiang-Jin Meng
Virginia Tech Vet. Med.
1410 Price's Fork Road
Blacksburg, VA 24061-0342

Deposited on Behalf of: Virginia Polytechnic Institute and State University

Identification Reference by Depositor:	**Patent Deposit Designation**
Chimeric Porcine Circovirus Type 1 (PCV1) and Type 2 (PCV2) infectious DNA clone: PCV1-2 Chimera	PTA-3912
Infectious DNA Clone of Type 2 Porcine Circovirus (PCV2): PCV2 Clone	PTA-3913
Type 2 Porcine Circovirus (PCV2): PCV2 #40895	PTA-3914

The deposits were accompanied by: __ a scientific description , a proposed taxonomic description indicated above. The deposits were received December 7, 2001 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested February 27, 2002 . On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris

Marie Harris, Patent Specialist, ATCC Patent Depository

Date: March 18, 2002

cc: Anne M. Rosenblum, Esq.
(Ref: Docket or Case No.: AM100878)